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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, QIAN J	

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 10/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/992,229	VANGURI ET AL.	
	Examiner	Art Unit	
	Q. Janice Li	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *3,10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 4-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 April 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election of Group I, claims 1-9, in Paper No. 10, and the species election of mouse and human as the first and second species respectively is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1, 2, 4, 5, and 7-9 read on the elected invention, however, upon search and consideration, claim 6 has been included and will be examined together with the elected species. Claims 3, 10, and 11 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Claims 1, 2, 4-9 are under current examination.

Priority

This application is a continuation-in-part of 60/248,812, filed 11/15/2000.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because the first named inventor has not signed the declaration in the space provided.

Drawings

The application contains two sets of figures, color photographs are identified in one set of the figures. Color photographs and color drawings are acceptable only for examination purposes unless a petition filed under 37 CFR 1.84(a)(2) is granted permitting their use as acceptable drawings. In the event that applicant wishes to use the drawings currently on file as acceptable drawings, a petition must be filed for acceptance of the color photographs or color drawings as acceptable drawings. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and an amendment to the first paragraph of the brief description of the drawings section of the specification which states:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the U.S. Patent and Trademark Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings have been satisfied.

The set of black and white figures are objected to because the supposed cells or stains could not be seen in the figures (figs. 1a-left panel, 1d-left panel, 1e, 1f, 2-left panel, 4, 7a-left panel, and 7b-mid panel).

Applicants are required to resubmit legible black and white figures or file a petition under 37 CFR 1.84(a)(2).

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1, 4, 6, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims are drawn to an immunocompetent post-natal animal, said animal encompasses human being, which is a non-statutory subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims are vague and indefinite because they recite a polynucleotide encoding an agent of interest, while "an agent" could be any chemical, a polynucleotide could only encode a peptide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1 and 7-9 are rejected under 35 U.S.C. 102(a) as being anticipated by *WO 00/49136*.

The claims are drawn to an immunocompetent post-natal animal of a first species having had administered thereto mesenchymal stem cells from an animal of a second species, wherein the cells may include at least one exogenous polynucleotide encoding an agent of interest and a method of making such comprising administering the MSC to an immunocompetent post-natal animal.

WO 00/49136 teach a method comprising administering mesenchymal stem cells encoding an immune system suppressor polypeptide to a subject in need thereof, including immunocompentent postnatal subject, wherein the MSCs could be xenogenic (abstract), wherein the MSC could be obtained from mouse, pig, sheep, cow, and the like (page 11, lines 3-9). Thus, *WO 00/49136* anticipates the instant claims.

Claims 1, 4, 5, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by *Azizi et al* (PNAS 1998;95:3908-13),and evidenced by *Pittenger et al* (Science 1999;284:143-7).

Azizi et al teach a method of transplanting human mensenchymal stem cells in the brain of immunocompetent post-natal albino rats, and the xeno-hybrid rats produced (e.g. fig. 3 and tab. 2). It is noted that *Azizi et al* use the term "MSCs (marrow stromal cells)", but clearly teach that the marrow stromal cells are also known as mesenchymal stem cells (1st paragraph, right column, page 3908). Moreover, *Azizi et al* use the same method as taught by *Pittenger et al* in obtaining the MSCs, thus the cells used by *Azizi et al* are indeed human mesenchymal stem cells. Accordingly, *Azizi et al* anticipate instant claims.

Claims 1, 4-9 are rejected under 35 U.S.C. 102(e) as being anticipated by *McIntosh et al* (US 6,368,636).

McIntosh et al teach a method comprising administering mesenchymal stem cells to an immunocompetent post-natal transplant recipient (abstract), wherein the MSCs could be autologous, allogeneic, or xenogenic to the recipient (column 2, lines 9-26), wherein the mesenchymal stem cells are engineered to express a polypeptide of interest, such as a death factor (column 8, lines 13-14). In the working examples, baboon or human mesenchymal stem cells were used for suppression of immune response across the species of human or baboon, respectively (Example 10). Therefore, *McIntosh et al* anticipate instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, 4-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over *McIntosh et al* (US 6,368,636), in view of *Azizi et al* (PNAS 1998;95:3908-13), and *Breitbart et al* (US 6,398,816).

Claim 2 is drawn to an immunocompetent post-natal mouse having human mesenchymal stem cells; claims 7 and 9 are drawn to using the mesenchymal stem cells for carrying exogenous gene of interest in making a xeno-hybrid animal.

As discussed in *§ 102*, *McIntosh et al* teach using mesenchymal stem cells for prevention and treatment of xenogenic immune response in transplantation. *McIntosh et al* focused on large animals such as dog, baboon as the recipient of the transplantation, and fail to specifically teach a mouse as the recipient. *McIntosh et al* further teach

transfecting the MSCs with a death factor, and do not elaborate on the gene that could be used for transfection.

Azizi et al teach a rat recipient for human MSCs in the study of in vivo behavior of MSCs. A rat belongs to rodent family, as is a mouse.

Breitbart et al teach using MSCs as a gene therapy carrier for variety of genes having therapeutic potentials (abstract and § II bridging columns 6-8).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combining or modifying the methods as taught by *McIntosh et al*, *Azizi et al,* and *Breitbart et al,* to generate a xeno-hybrid mouse or any other mammal having human mesenchymal stem cells and carrying an exogenous gene, with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because rat and mouse are the most used laboratory animals for research purpose. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 9:30 am - 6 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JANICE LI
PATENT EXAMINER

Q. Janice Li
Patent Examiner
Art Unit 1632

QJL
October 17, 2003